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Fanelli Strain & Haag PLLC
1455 Pennsylvania Ave., N.W.
Suite 400
Washington, D.C. 20004

In Re: Patent Term Extension
Application for
U.S. Patent No. 6,869,939

NOTICE OF FINAL DETERMINATION — INELIGIBLE

This is in response to the application for extension of the term of U.S. Patent No. 6,869,939 ("the '939 patent") filed under 35 U.S.C. § 156 in the United States Patent and Trademark Office ("USPTO") on February 17, 2009 ("the PTE Application"). Prism Pharmaceuticals, Inc. ("Applicant"), exclusive licensee of the '939 patent, filed the PTE Application. Applicant seeks extension based upon the December 24, 2008 premarket approval of NEXTERONE® (amiodarone hydrochloride) under Section 505 of the Federal Food Drug and Cosmetic Act ("FFDCA"). Because the Food and Drug Administration ("FDA") and the USPTO have determined that the December 24, 2008 approval of NEXTERONE® (amiodarone hydrochloride) does not constitute the first permitted commercial marketing or use of the "product" under Section 505 of the FFDCA, the PTE Application is **dismissed**.

A single request for reconsideration of this FINAL DETERMINATION OF INELIGIBILITY may be made if filed by the applicant within TWO MONTHS of the mailing date of this letter. The period for response may be extended pursuant to 37 C.F.R. 1.136. *See*, 37 C.F.R. 1.750. A failure to respond to this letter will result in the application papers being placed into the patent file with no further action taken on the application for patent term extension. Thus, no further correspondence will be sent to Applicant.

A. Factual Background

On March 22, 2005, the USPTO granted the '939 patent to Gerold L. Mosher et al., who assigned their rights to Cydex, Inc.

On December 24, 2008, the FDA approved NDA No. 22-325 for NEXTERONE® (amiodarone hydrochloride).

On February 17, 2009, Applicant timely filed the PTE Application in the USPTO.

On March 31, 2009, the USPTO mailed a letter to FDA, requesting the FDA's assistance in confirming that (1) the product identified in the PTE Application, NEXTERONE® (amiodarone hydrochloride), was subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first permitted commercial marketing or use and (2) the PTE application was filed within the sixty-day period beginning on the date the product received permission under the provision of law under which the applicable regulatory review period

occurred for commercial marketing or use, as required by 35 U.S.C. § 156(d)(1).

On September 30, 2009, FDA responded to the USPTO stating (1) FDA's approval of NEXTERONE® (amiodarone hydrochloride) does not represent the first permitted commercial marketing or use of the "product," as defined under 35 U.S.C. § 156(f)(1), and (2) the PTE Application was timely filed.

B. Decision

1. The plain language of 35 U.S.C. § 156(f) shows that NEXTERONE® (amiodarone hydrochloride) is not the first permitted commercial marketing or use of the "product" as required by 35 U.S.C. § 156(a)(5)(A)

Section 156(a) of Title 35 sets forth several requirements that must be met before the Director can extend the term of a patent. *See* 35 U.S.C. §§ 156 (a)(1)-(a)(5), (d)(1), & (e)(1). Section 156(a)(5)(A) requires that:

> the permission for the commercial marketing or use of the product ... [be] the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

(Emphasis added). The term "product" as used in section 156(a)(5)(A) is defined in section 156(f)(1) as a "drug product," and the term "drug product" is defined in section 156(f)(2) as the "active ingredient of [a] new drug, antibiotic drug, or human biological product ... including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient." 35 U.S.C. § 156(f)(2)(A).

It is undisputed that amiodarone hydrochloride is the active ingredient of Applicant's NEXTERONE® drug product. In response to the requirement of 37 C.F.R. § 1.740(a)(4) to identify each active ingredient in the product, the PTE Application identifies one and only one active ingredient. Specifically, the PTE Application at page 5 identifies amiodarone hydrochloride as "[t]he active ingredient of the product NEXTERONE®." This is consistent with the results from a Detail Record Search for NEXTERONE® in the electronic Orange Book, as accessed on March 20, 2009 (a copy of the printout is attached), which also identifies amiodarone hydrochloride as the sole active ingredient of NEXTERONE®. It is also consistent with the FDA's September 30, 2009 letter to the USPTO.

It is also undisputed that amiodarone hydrochloride was approved by the FDA under section 505 of the FFDCA prior to the December 24, 2008 approval of NEXTERONE®. The PTE Application at page 5 states that "[t]he active ingredient, amiodarone hydrochloride, was approved by the FDA on December 24, 1985 in NDA 18-972 for the product CORDARONE® ... under Section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(b))." In addition, an Active Ingredient Search for amiodarone hydrochloride in the electronic Orange Book, as accessed on March 20, 2009 (a copy of the printout is attached), identifies a host of

other NDA's (and ANDA's) approved prior to the present approval of NEXTERONE® in which the active ingredient is amiodarone hydrochloride. Further, the FDA's September 30, 2009 letter states that:

> [t]he active ingredient in Nexterone (amiodarone hydrochloride) has been previously approved for commercial marketing or use under section 505 of the Federal Food, Drug, and Cosmetic Act. Previous approvals include Cordarone (Wyeth Pharmaceuticals), NDA 18-972, Amiodarone Hydrochloride (International Medication Systems), NDA 21-594, and many other generic equivalent products.

Accordingly, the later approved NEXTERONE® (amiodarone hydrochloride) does not represent the first permitted commercial marketing or use of the "product" under the provision of law under which such regulatory review occurred.

The present facts are completely analogous to the facts in *Fisons v. Quigg*, 1988 WL 150851 (D.D.C. 1988) ("*Fisons I*"), which the Federal Circuit affirmed in *Fisons v. Quigg*, 876 F.2d 99 (Fed. Cir. 1989) ("*Fisons II*") (collectively, "the *Fisons* cases"). Just as it is undisputed here that amiodarone hydrochloride is the active ingredient of Applicant's NEXTERONE® drug product, it was undisputed in the *Fisons* cases that cromolyn sodium was the active ingredient of the products at issue in the *Fisons* cases. *See, e.g., Fisons I* at *2 and *3. Just as the Federal Circuit in *Fisons II* affirmed at 876 F.2d 99, 100 "that because Fisons' patented new products containing cromolyn sodium did not qualify as the first permitted commercial marketing or use of the active ingredient cromolyn sodium, extensions of the patent term for the subject patents were not permissible," the USPTO here concludes that the PTE Application does not satisfy the requirement of section 156(a)(5)(A) and the '939 patent is ineligible for a patent term extension. Thus, the PTE Application must be **dismissed**.

2. Applicant's statement that "sulfobutyl ether β-cyclodextrin-amiodarone hydrochloride complex was not previously approved prior to the approval of NEXTERONE®" is irrelevant

The PTE Application at page 5 states that NEXTERONE® "is a sulfobutyl ether β-cyclodextrin-amiodarone hydrochloride intravenous solution." The PTE Application at page 5 further states that "[t]he sulfobutyl ether β-cyclodextrin-amiodarone hydrochloride complex was not previously approved prior to the approval of NEXTERONE®."

However, as already stated, it is undisputed that amiodarone hydrochloride is the active ingredient of Applicant's NEXTERONE® drug product. The sulfobutyl ether β-cyclodextrin component is not identified as an active ingredient of NEXTERONE® by the electronic Orange Book. Indeed, the PTE Application itself does not identify

sulfobutyl ether β-cyclodextrin as an active ingredient of NEXTERONE®. Accordingly, whether sulfobutyl ether β-cyclodextrin-amiodarone hydrochloride complex has been previously approved prior to the approval of NEXTERONE® is irrelevant to the determination of whether the requirement of section 156(a)(5)(A) has been fulfilled.

Further, the PTE Application at page 6 states that "[t]he sulfobutyl ether β-cyclodextrin component has previously been combined with" each of voriconazole, ziprasidone mesylate, aripiprazole, and maropitant citrate. According to page 6 of the PTE Application, each of these previous combinations of the sulfobutyl ether β-cyclodextrin component has been previously approved by the FDA. Consequently, even if Applicant is somehow trying to base the eligibility of the '939 patent for term extension on NEXTERONE® having two active ingredients (sulfobutyl ether β-cyclodextrin and amiodarone hydrochloride), such an argument would be unpersuasive. It is the Office's long-standing position that if a drug product contains two active ingredients, each of which has been previously approved individually, then regulatory approval of the combination drug product cannot be the basis for extension of a patent claiming the approved combination. *See In re Alcon Labs Inc.*, 13 USPQ2d 1115, 1118 (Comm'r of Pats. 1989) ("For a product which contains a plurality of active ingredients, as here, the statute [referring to 35 U.S.C. § 156(a)(5)(A)] must be analyzed with respect to each active ingredient."). The Federal Circuit confirmed that the Office's position is correct in *Arnold Partnership v. Dudas*, 362 F.3d 1338, 1343 (Fed. Cir. 2004).

For the reasons stated herein, the USPTO concludes that the PTE Application does not satisfy the requirement of section 156(a)(5)(A) and the '939 patent is ineligible for a patent term extension. Therefore, the PTE Application must be **dismissed**.

C. Conclusion

For the reasons stated above, Applicant's request for extension of the patent term of the '939 patent is **dismissed**.

Any correspondence with respect to this matter should be addressed as follows:

By mail: Mail Stop Hatch-Waxman PTE
P.O. Box 1450
Alexandria, VA 22313-1450

By FAX: (571) 273-7728

Telephone inquiries related to this determination should be directed to Raul Tamayo at (571) 272-7728.

Mary Till
Legal Advisor
Office of Patent Legal Administration
Office of the Associate Commissioner
for Patent Examination Policy

cc: Office of Regulatory Policy
Food and Drug Administration
10903 New Hampshire Ave.
Bldg. 51, Room 6222
Silver Spring, MD 20993-0002

Attention: Beverly Friedman

RE: NEXTERONE® (amiodarone hydrochloride)
Docket No.: FDA-2009-E-0240

Search results from the "OB_Rx" table for query on "022325."

Active Ingredient:	AMIODARONE HYDROCHLORIDE
Dosage Form;Route:	INJECTABLE; INJECTION
Proprietary Name:	NEXTERONE
Applicant:	PRISM PHARMS
Strength:	50MG/ML
Application Number:	022325
Product Number:	001
Approval Date:	Dec 24, 2008
Reference Listed Drug	No
RX/OTC/DISCN:	RX
TE Code:	**AP**

Patent and Exclusivity Info for this product: View

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Patent and Generic Drug Product Data Last Updated: March 20, 2009

Active Ingredient Search Results from "OB_Rx" table for query on "amiodarone hydrochloride."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
075761	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	ABRAXIS PHARM
076232	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	AKORN
076394	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	APOTEX INC
076018	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	BEDFORD
076299	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	BEDFORD LABS
076217	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	BIONICHE PHARMA
077161	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	GLAND PHARMA LTD
077234	AP	No	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	HIKMA FARMACEUTICA
075955	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	HOSPIRA
021594	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	INTL MEDICATION SYS
022325	AP	No	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	NEXTERONE	PRISM PHARMS
076163	AP	Yes	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	TEVA PARENTERAL
077834	AP	No	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	WOCKHARDT
077610	AP	No	AMIODARONE HYDROCHLORIDE	INJECTABLE; INJECTION	50MG/ML	AMIODARONE HYDROCHLORIDE	WOCKHARDT
075188	AB	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	ALPHAPHARM

078578 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	APOTEX CORP
077069 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	AUROSAL PHARMS
077069 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	400MG	AMIODARONE HYDROCHLORIDE	AUROSAL PHARMS
075389 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	BARR
075315 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	SANDOZ
075315 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	400MG	AMIODARONE HYDROCHLORIDE	SANDOZ
075424 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	100MG	AMIODARONE HYDROCHLORIDE	TARO
075424 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	TARO
076362	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	300MG	AMIODARONE HYDROCHLORIDE	TARO
076362 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	400MG	AMIODARONE HYDROCHLORIDE	TARO
074739 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	TEVA PHARMS
075135 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	100MG	PACERONE	UPSHER SMITH
075135 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	PACERONE	UPSHER SMITH
018972 **AB**	Yes	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	CORDARONE	WYETH PHARMS INC
079029 **AB**	No	AMIODARONE HYDROCHLORIDE	TABLET; ORAL	200MG	AMIODARONE HYDROCHLORIDE	ZYDUS PHARMS USA INC

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